REMARKS

Bayer, the assignee of the present application, submits this amendment under 37 C.F.R. § 1.116(b) and under 37 C.F.R. § 1.116(c). The amendments to claims 8 and 11 present the rejected claims in better form for consideration on appeal. The amendments to claim 8 are also necessary to elucidate the difference between the invention and U.S. Patent No. 6,024,981 to Khankari et al. ("Khankari"). The Examiner's reliance upon newly cited Khankari could not have been earlier addressed, and the amendments and remarks set forth herein may forestall the need for an appeal.

The Examiner has rejected all the pending claims under 35 U.S.C. § 102. The product claims, claims 8-10 were rejected over Khankari, and the method claims, claims 11-15, were again rejected over GB Patent No. 2,307,857 to Leslie et al. ("Leslie"). Applicant respectfully requests reconsideration of these rejections for the following reasons.

The claimed invention is directed to effervescent compositions with improved stability and to methods of making these compositions. Applicant has discovered that product stability is improved by incorporating at least one member of the effervescent couple in a dispersion of a fusible sugar, sugar alcohol or sugar substitute. The "dispersion" of the invention requires more than simple physical mixing of granulated or powdered ingredients. The fusible sugar, sugar alcohol or sugar substitute should be at

least partially melted to form a molten material into which at least one member of an effervescent couple is dispersed. A "dispersion" thus means a solution, blend, suspension, emulsion or other intimate and thorough combining of at least one member of the effervescent couple and the fusible sugar, sugar alcohol or sugar substitute so as to prevent the premature reaction of the effervescent couple.

The compositions of the claimed invention comprise an effervescent couple. The compositions further comprise a pharmaceutically active substance, and a fusible sugar, sugar alcohol, or sugar substitute. Either member of the effervescent couple, or both, may be dispersed in the molten sugar, sugar alcohol, or sugar substitute.

The Examiner has rejected claims 8-10 under 35 U.S.C. § 102 (b), based on U.S. Patent No. 6,024,981 to Khankari et al. ("Khankari"), citing Example 1 at column 15 and the disclosure at column 14, lines 44-65. The Examiner has rejected claims 11-15 under 35 U.S.C. § 102 (b), based on UK Patent No. 2,307,857 to Leslie et al. ("Leslie").

The product claims, claims 8-10, require a stabilizing amount of a fusible sugar, sugar alcohol, or sugar substitute sufficient to disperse at least one member of the effervescent couple. The claims also require that at least one member of the effervescent couple actually be dispersed in the fusible sugar, sugar alcohol, or sugar substitute. The distinction between the dispersion of the claimed invention and direct compression of ingredients without formation of the dispersion found in the cited references is the source of the improved stability of the invention. In direct compression, granules of each

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member of an effervescent couple can find themselves in contact under high pressure. This close proximity can lead to early reaction and instability of the final product. On the other hand, even if a granule of a dispersed member of an effervescent couple finds itself in close proximity with the other member of the effervescent couple, any reaction will be substantially reduced because of the relatively lower concentration of the first member in the dispersion granule. Thus, the structure of the claimed invention differs significantly from the structure obtained from direct compression.

The claimed requirements are neither taught nor suggested by Khankari. Khankari is directed to a quick dissolve tablet made with a non-direct compression filler. Although effervescent agents may be present in Khankari's tablet, the method of manufacture of the tablet is direct compression. As stated at column 11, lines 32-41, "The method includes the steps of forming a mixture . . . and compressing the mixture to form . . . tablets . . .. Preferably, tablets are formed by 'direct compression.' 'Direct compression' as used herein means that one can avoid the difficulty and expense of a wet or dry granulation prior to compression." All ten examples in Khankari use direct compression without any melting of a sugar before compression. The relatively low compression strength of Kahnkari (20-50N) will not form a melt of a fusible sugar, sugar alcohol or sugar substitute. One skilled in the art would simply not find the structure, or the stability, of the claimed invention in Kahnkari, and Khankari cannot teach or suggest the claimed invention.

* But cls. 8-10 are drawn to product claims - therefore, the process cls of Khankari is irrelevant. Appls argue the process - not persuasive over 102 (e) rej. cls, 8-10. Maintain rej.

The Examiner also rejected claims 11-15 over Leslie. Leslie is directed to an effervescent composition containing tramadol, an analgesic with an unpleasant taste. Leslie reports that "[w]e have surprisingly found that a formulation containing tramadol or pharmaceutically acceptable salt thereof and an acid/base couple, when dissolved in an appropriate amount of water, is of surprisingly acceptable palatability with an unexpectedly low degree of bitterness even in the absence of sweeteners." (Page 2, lines 24-28.) Leslie concerns itself only with flavor. Stability is not the objective of Leslie, and Leslie concedes that any "conventional" method may be used to make its tramadol product, including a process in which the "tramadol . . . and the components of the acid base couple may be simply dry mixed and compressed to form tablets." (Page 2, lines 30-32.) In a preferred process, polyethylene glycol (PEG) of molecular weight 1,000 to 20,000 is added as a binder, and Leslie's materials are physically mixed via mechanical action at an elevated temperature.

Leslie, however, does not teach or suggest the process of claims 11-15. PEG is not a fusible sugar, sugar alcohol or sugar substitute as required by claims 11-15. The presence of this ingredient cannot teach or suggest the process of claims 11-15. Moreover, Leslie uses very low, or even no, amounts of sweetener in its examples. The highest amount of sweetener actually used in Leslie is 5 mg or 0.22 weight percent of the formulation (Example 1). This amount of sweetener is matched with 990 mg of citric acid (43.27 weight percent of the formulation) and 1,243 mg carbonate (54.33 weight percent). The amount of sugar in the Leslie formulation would not lead to a stabilized

Appls. argue but do not claim.

medicament, especially since Example 1 physically mixes all the ingredients and feeds them to a tablet press.

Example 3, the example cited by the Examiner in the first office action, does not teach or suggest the claimed invention. Saccharin comprises only 0.2 weight percent of the formulation, while the citric acid comprises 39 weight percent of the formulation and the carbonates comprise 49 weight percent of the formulation. Thus, as with Example 1, the result would not be a stabilized medicament, and there is no at least partially molten blend formed with an ancillary substance. Leslie cannot teach or suggest dispersion of one or both parts of an effervescent couple in a fusible sugar, sugar alcohol or sugar substitute simply because Leslie does not have enough sugar substitute to form a dispersion. Instead, Leslie relies on polyethylene glycol to act as a binder.

The Examiner points to the discussion of Leslie regarding the temperature of extrusion of about 60° C. That temperature is, however, designed to drive out free moisture from Leslie's blend. There is no teachingor suggestion that a melt is, or should be, formed. Indeed, Leslie incorporates the ingredients in the effervescent couple at different points in the mechanical working of the powder blends to reduce premature reaction. Thus, there can be no anticipation of claims 11-15 by Leslie.

The Examiner points to page 5, lines 5-11 of the patent application to bolster the anticipation rejection, arguing that the method of Leslie is equivalent to the claimed process. This cited language, however, does not show equivalence to Leslie. Rather this

language shows that the process of claim 11 is not limited to a specific order of steps. The steps of adding the remaining ingredients and cooling the blend need not be carried out in the recited order to achieve a stabilized product. If the process is carried out in one way, the stabilized product will have only one half of the effervescent couple in the cooled melt and the remaining ingredients outside of the melt. If the process is carried out in a different order, the stabilized product will have both halves of the effervescent couple protected in the melt with the remaining ingredients outside the melt. Or, all the ingredients, including the remaining ingredients, may be inside the melt.

The examiner also argues that the intended use of the product is irrelevant to the process. As claimed, however, claim 11 requires the step of forming a stabilized medicament. The step of forming is not an intended use, but an integral part of the claim.

In view of the arguments set forth above and the claim amendments presented herein, Applicants respectfully submit that the pending claims are in condition for allowance. Reconsideration is respectfully requested. The Examiner is invited to call the undersigned attorney at 973 408-8229 with any questions.

Respectfully Submitted,

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